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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,748	SUTHERLAND, JOHN W.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/6/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's amendment filed December 1, 2004 is acknowledged and has been entered. Claim 1 has been amended. Claims 1, 5, 8, 9, 12, 13, and 15 have been amended. Claims 2-3 and 18-20 have been canceled. Claims 1, 4-17 are pending. All of the arguments have been thoroughly reviewed and considered but are not moot in view of the new grounds of rejection necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Ground(s) of Rejection

THE NEW GROUND(S) OF REJECTIONS ARE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 13, 15, 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Gattermann et al (Leukemia, vol. 9, No. 10, pages 1704-1710, October 1995). Regarding claim 1, 13, 15 and 16, Gattermann et al teach a method of detecting mutant mtDNA comprising (a)

contacting a sample comprising mtDNA with mutant PCR primers, amplifying the product of step (a) under short PCR conditions and (c) identifying the presence of amplicons of step (b), wherein the presence of such amplicons is indicative of the presence of nucleic acid deletion sequences is greater than 4kb and further quantitating the presence of the amplicons by comparison with a wild-type (control) standard (abstract and section entitled "Materials and Methods, page 1704-05). Therefore, Gattermann et al meets the limitations of claims 1, 13, 15 and 16 of the instant invention.

5. Claims 1, 13, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Marin-Garcia et al (Cardiovascular Research, vol. 31, pages 306-313, 1996). Regarding claim 1, Marin-Garcia et al teach a method of detecting mutant mtDNA comprising (a) contacting a sample comprising mtDNA with mutant PCR primers, (b) amplifying the product of step (a) under short PCR conditions, and (c) identifying the presence of amplicons of step (b), wherein the presence of such amplicons is indicative of the presence of nucleic acid deletion sequences equal to or greater than 4kb and further quantitating the presence of the amplicons by comparison with a wild-type standard (abstract, page 307, section entitled "Methods" and Table 1 and page 309, section 2.1.1.7 at col. 2). Therefore, Marin-Garcia et al meets the limitations of claims 1, 13, 15 and 16 of the instant invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 4, 5, 7, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gattermann et al (Leukemia, vol. 9, No. 10, pages 1704-1710) in view of Herrnstadt et al (US 6,027,883, February 2000) and further in view of Todd et al (WO 96/32500, October 1996) Regarding claims 4, 5, 7, 11 and 14, Gattermann et al teach a method of detecting mutant nucleic acid comprising contacting a sample comprising mitochondrial DNA with mutant PCR primers; amplifying the product of step (a) under short PCR conditions and identifying the presence of amplicons of step (b), wherein the presence of such amplicon is indicative of the presence of a deletion mutation greater than 4kb and further quantitating the presence of the amplicons by comparison with a wild-type (control) standard (Abstract and materials and methods). Gatterman et al differs from the instant invention in that the reference does not expressly teach

contacting the sample with a cleavage reagent or wherein the primers are designed to detect the mutant target sequence in the sample along with the addition of four different nucleotide triphosphates and a DNA polymerase under conditions such that the DNA is amplified and detecting the amplicon.

Hernstadt et al teach a method similar to that of Gattermann et al for detecting mutant mt-DNA, the method comprising the steps of contacting a sample comprising mitochondrial DNA with mutant PCR primers; amplifying the product of step (a) under short PCR conditions and identifying the presence of amplicons of step (b) and further quantitating the presence of the amplicons by comparison with a wild-type standard (col. 7, lines 15-22, col. 19, lines 34-53, and col. 31, line 42 to col. 34, line 47). Herrnstadt et al additionally teach wherein primers were designed, e.g., forward and reverse primers, to detect the mutant target sequences in the sample along with the addition of four different nucleoside triphosphates and a DNA polymerase under conditions such that the DNA is amplified and detecting the amplicons (see col. 31-33).

Herrnstadt et al. differs from the instant invention in that Herrnstadt et al do not expressly teach wherein a cleavage reagent is contacted in the samples containing a mixture of mutant DNA and wild type DNA such that only the mutant DNA is amplified preceding the addition of each of four different nucleoside triphosphates and a DNA polymerase.

In a method similar to that of Herrnstadt et al for detecting a mutant nucleic acid sequence, Todd et al. discloses a method comprising the steps of: contacting a sample suspected of containing a mutation, wherein said mutation is an insertion, deletion or point mutation, with a cleavage agent, contacting the sample with mutant PCR primers; amplifying the product under short PCR conditions in the presence of four different nucleoside triphosphates and a DNA

polymerase, such that only the mutant DNA is amplified and detecting the presence of the amplified DNA (see pages 4-6). Todd et al teaches that the use of a cleavage agent in the PCR method is advantageous because it results in the exclusive amplification of a mutant sequence (page 6, lines 3-5).

Therefore, in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the PCR detection method of Gattermann et al in view of Herrnstadt et al to incorporate a cleavage reagent as disclosed by Todd et al for the advantage of exclusively amplifying mutant target sequences as suggested by Todd et al.

9. Claim 6, 8, 10, 12, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gattermann et al in view of Herrnstadt et al in view of Todd et al as previously applied above and further in view of Whitcome et al. (Clinical Chemistry, Vol. 44, No. 5, pages 918-923, 1998). Regarding claims 6, 8, 10, 12 and 17, Gattermann et al in view of Herrnstadt et al in view of Todd et al. teach a method for detecting and quantifying mutant nucleic acid using short PCR conditions. The references differ from the instant invention in that they do not teach wherein the method further comprises the step of contacting the samples with probes wherein said probes are selected from TAQMAN probes, molecular beacon probes, PNA probes, DNAZYMES or combination thereof. Nor does the references teaches wherein the nucleic acid is quantitated by real-time monitoring.

In a general teaching, Whitcombe et al. teach the use of a fluorescent assay for PCR amplicons. Whitcombe et al teaches that the method utilizes a single TAQMAN probe for the

detection of any one target DNA sequence or a single pair of probes for genotyping any bi-allelic polymorphism in a PCR reaction for the quantitation of amplicons. Whitcombe et al teach that the method is useful for the single tube genotype analysis of a variety of human DNA polymorphisms and mutations (Abstract). Therefore in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the PCR mutation detection method of Gattermann et al in view of Herrnstadt et al in view of Todd et al to encompass a TAQMAN probe(s) followed by quantitating by real-time monitoring. One of ordinary skill in the art would have been motivated to do for the advantage taught by Whitcome that the method is useful for the single tube genotype analysis of a variety of human DNA polymorphisms and mutations.

Conclusion

10. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
9/11/05